REMARKS

The attached Appendix shows the changes to the amended paragraphs. The amended paragraphs and amended Sequence Listing are supported by the present specification as discussed below.

Sequence Compliance

The Examiner noted that some SEQ ID NOs were not identified in the specification. Action at page 2. Applicants amended the specification to include SEQ ID NOs. All of the sequences were previously disclosed. Therefore, the amendment adds no new matter.

Applicants also amended the specification to include a new sequence listing. The amended sequence listing includes four sequences (SEQ ID NOs: 36-39) that were disclosed in the specification at pages 22, 97, and 111, but were not included in the original sequence listing. Because SEQ ID NOs 36-39 were disclosed in the specification, the amendment adds no new matter.

An amended substitute copy of the computer readable form (CRF) of the Sequence Listing and an amended substitute paper copy of the Sequence Listing are enclosed. Based on representation from Clifford Ford, an attorney at Finnegan, Henderson et al., the undersigned states that the information contained in the CRF of the Sequence Listing is identical to the Paper Copy of the Sequence Listing (30 pages), and that the Sequence Listing adds no new matter.

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Drawings

The drawings were objected to under 37 C.F.R. 1.84. Action at page 2. Substitute drawings are being filed with the Correction of Informalities to Drawings.

Restriction Requirement

Applicants thank the Examiner for reconsideration and partial withdrawal of the prior restriction requirement. In the present Action, the Examiner required restriction to one of 37 groups of claims under 35 U.S.C. § 121. Without listing each individual group and the corresponding subject matter, Applicants summarize the restriction requirement as follows:

Groups I-II (Claims 1-7) which the Examiner contends are directed to isolated nucleic acid sequences, vectors, host cells and methods of producing the polypeptide.

Groups III-IV (Claims 8-12 and 19-23) which the Examiner contends are directed to polypeptides, fragments and compositions thereof.

Groups V-VI (Claims 13-18), which the Examiner contends are directed to an antibody or fragment thereof.

Groups VII-VIII (Claim 24), which the Examiner contends are directed to a method of treating or preventing a T cell mediated disorder.

Groups IX-X (Claim 25), which the Examiner contends are directed to a method of diagnosing a T cell mediated disorder.

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Groups XI-XII (Claims 26-27), which the Examiner contends are directed to a method of identifying a test molecule that binds to a polypeptide.

Groups XIII-XIV (Claim 28), which the Examiner contends are directed to a method of regulating T cell activation by administering a nucleic acid.

Groups XV-XVI (Claim 29), which the Examiner contends are directed to a transgenic non-human mammal.

Groups XVII-XXII (Claims 30-38), which the Examiner contends are directed to a method of suppressing an immune response/IgE production or a method of decreasing IgE production.

Groups XXIII-XXXVII (Claims 39-42), which the Examiner contends are directed to a method of enhancing an immune response.

Applicants elect Group IV, claims 8, 10, 12, and 19-23, "drawn to a polypeptide related to B7RP1, encoded by SEQ ID NO: 1 [or 11 or 16], fragments and compositions thereof, and heterologous proteins comprising said polypeptide." The Examiner omitted SEQ ID NOs: 11 or 16 in the description of Group IV on page 4 of the Action. Those sequences, however, are included in the independent claims from which the claims of Group IV depend. Moreover, the election requirement at ¶ 15 of the Action makes clear that the Examiner recognized that those sequences were included in the claims of Group IV.

In view of Applicants' election of Group IV, the Examiner has required election of a single disclosed species. Applicants elect SEQ ID NOs. 12 and 17. Applicants

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respectfully remind the Examiner that, in the event that the elected species is found allowable, the Examiner is required to examine the claims with respect to the non-elected species. *See* MPEP §809.02(c)(B)(1).

If there is any fee due in connection with the filing of this Response, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

Dated: October 7, 2002

By: Robert W. Mann Reg. No. 48,595 for
M. Paul Barker
Reg. No. 32,013

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APPENDIX

Paragraph beginning at page 5, line 9, and ending at page 5, line 11:

b) the nucleotide sequence encoding the polypeptide as set forth in Figure 2A (SEQ ID NO: 6) from residues 1-322 or from residues 47-322 or as set forth in Figure 3A (SEQ ID NO:11) from residues 1-288 or from residues 19-288, 20-288, 21-288, 22-288, 24-288, or 28-288; or as set forth in Figure 12A **(SEQ ID NO: 16)** from residues 1-302 or from residues 19-302, 20-302, 21-302, 22-302, 24-302 or 28-302;

Paragraph beginning at page 21, line 33, and ending at page 22, line 16:

CD28 related protein-1, or CRP1, is predicted to be a type I transmembrane protein with a signal sequence and extracellular domain at the amino-terminus, a transmembrane domain, and a carboxy terminal intracellular domain (Figure 1). The full-length CRP1 protein is 180 amino acids in its mature form. The predicted leader sequence spans about amino acid residues 1-20 (relative to the initiating methionine) and the extracellular domain of the mature protein encompasses about residues 21-145 (Example 1). The predicted transmembrane domain spans about residues 146-163 and the intracellular domain encompasses about residues 164-200. The amino terminal extracellular domain is similar to an Ig loop with conserved putative intra- and inter-molecular bonding cysteines. Furthermore, a "MYPPPY" motif **(SEQ ID NO: 36)**, which is previously known to be important for B7.1 and B7.2 binding to CD28 and CTLA-4, is also partially conserved.

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Paragraph beginning at page 22, line 29, and ending at page 23, line 7:

Human CRP1 is a transmembrane protein having the nucleotide and amino acid sequence as shown in Figure 13A **(SEQ ID NOs: 21 and 22, respectively)**. The predicted leader sequence spans about residues 1-19 or about residues 1-20. The predicted mature amino terminus is at residues 20 or 21. Preferably, the mature amino terminus is at position 21. The extracellular domain spans from any of the prediced mature amino termini to about amino acid residue 140, the transmembrane domain spans about residues 141-161 and the intracellular domain spans about residues 162-199. Human CRP1 protein has 69% identity to the murine protein and the corresponding nucleotide sequences are 77% identical. The sequence of human CRP1 was reported in Hutloff et al. Nature 397, 263-266 (1999).

Paragraph beginning at page 41, line 30, and ending at page 42, line 6:

The term " CRP1 or B7RP1 polypeptide" refers to a polypeptide having the amino acid sequence of Figure 1A (SEQ ID NO:2), Figure 2A (SEQ ID NO:7) or Figure 3A (SEQ ID NO:12)**, or FIGURE 12A (SEQ ID NO: 17), OR FIGURE 13A (SEQ ID NO: 22)** and all related polypeptides described herein. Related polypeptides includes allelic variants, splice variants, fragments, derivatives, substitution, deletion, and insertion variants, fusion polypeptides, and orthologs. Such related polypeptides may be mature polypeptides, *i.e.*, polypeptide lacking a signal peptide. A CRP1 or B7RP1 polypeptide may or may not have amino terminal methionine, depending on the manner in which they are prepared.

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Paragraph beginning at page 42, line 7, and ending at page 42, line 24:

The term "CRP1 or B7RP1 polypeptide fragment" refers to a peptide or polypeptide that is less than the full length amino acid sequence of a CRP1 or B7RP1 polypeptide as set forth in Figure 1A (SEQ ID NO:2), Figure 2A (SEQ ID NO:7) or Figure 3A (SEQ ID NO:12)**, or FIGURE 12A (SEQ ID NO: 17), OR FIGURE 13A (SEQ ID NO: 22)**. Such a fragment may result from truncation at the amino terminus, truncation at the carboxy terminus, and/or a deletion internal to the polypeptide sequence. Such CRP1 or B7RP1 polypeptides fragments may be prepared with or without an amino terminal methionine. In addition, CRP1 or B7RP1 polypeptides fragments may be naturally-occurring splice variants, other splice variants, and fragments resulting from naturally occurring *in vivo* protease activity. Preferred CRP1 or B7RP1 polypeptide fragments include soluble forms of CRP1 or B7RP1 which lack a functional transmembrane domain and comprise part or all of the extracellular domain of either CRP1 or B7RP1.

Paragraph beginning at page 42, line 25, and ending at page 42, line 36:

The term "CRP1 or B7RP1 polypeptide variants" refers to CRP1 or B7RP1 polypeptides whose amino acid sequences contain one or more amino acid sequence substitutions, deletions, and/or additions as compared to the CRP1 or B7RP1 polypeptides amino acid sequences set forth in Figure 1A (SEQ ID NO:2), Figure 2A (SEQ ID NO:7) or Figure 3A (SEQ ID NO:12)**, or Figure 12A (SEQ ID NO: 17), or Figure 13A (SEQ ID NO: 22)**. Such CRP1 or B7RP1 polypeptides variants can be prepared from the corresponding CRP1 and B7RP1 polypeptides nucleic acid molecule

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variants, which have a DNA sequence that varies accordingly from the DNA sequences for CRP1 or B7RP1 polypeptides.

Paragraph beginning at page 97, line 19, and ending at page 98, line 5:

A cDNA clone containing an open reading frame of 199 amino acids was obtained (Figure 13A). This cDNA clone contained nucleotide and amino acid homologies to the murine CRP1 clone described in Example 1 and Figure 1. The nucleotides corresponding to the open reading frame of this human clone was 77% identical to the murine CRP1 gene. Translation of the human sequence and subsequent comparison with the murine CRP1 protein revealed 69% amino acid identity with the murine protein (Figure 13B). In addition, the motif between amino acids 114 to 119, "FDPPPF" **(SEQ ID NO: 37)**, was conserved between the murine and human CRP1 genes. This motif corresponds to the "MYPPPY" **(SEQ ID NO: 36)** motif in murine and human CD28 that is essential for B7 protein interaction. Furthermore, the cysteines at amino acid positions 42, 109, and 141 are also conserved. These cysteines correspond to cysteines in CD28 and CTLA-4 at are involved in Ig loop formation and intermolecular disulfide dimerization. The close similarity with murine CRP1, and structural similarities with the CD28 homology family, indicate that this is the human CRP1 homolog.

Paragraph beginning at page 111, line 13, and ending at page 112, line 6:

The CRP1 gene in mice was disrupted by deleting a genomic fragment corresponding to nucleotides 318-591 of the murine CRP1 cDNA sequence(see SEQ ID NO:1). The murine CRP1 gene was isolated from a 129J library using the full-length

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(800 bp) cDNA probe (Yoshinaga et al. Nature 402, 827-832 (1999). The targeting vector, which replaced a 2.8kb genomic fragment with a neomycin resistance (neo) cassette in sense orientation relative to CRP1 transcription, was electroporated into E14 embryonic stem (ES) cells (129/Ola, available from the American Type Culture Collection, Manassas, Va under accession no. CRL-1821). After G418 selection, homologous recombinants were identified by PCR using the primer pair GAG ACT CAT GCT GTG GTT TCA GG (SEQ ID NO: **38**) and TTC GCC AAT GAC AAG ACG CTG G (SEQ ID NO: **39**) and verified by Southern blotting. Chimeric mice generated from $CRP1^{+/-}$ ES clones were crossed with C57BL6 females to produce $CRP1^{+/-}$ mice. Germline transmission of the CRP1 mutation was assessed by PCR and Southern blot analysis of tail DNA. $CRP1^{-/-}$ mice generated by the intercrossing of heterozygous offspring were born at the expected Mendelian frequency and were viable, fertile and of normal size. To verify that the CRP1 mutation had abolished CRP1 expression, activated T-cells from $CRP1^{-/-}$ mice and control littermates were analyzed by flow cytometry. Upon in vitro T-cell activation, CRP1 was expressed on the surface of both $CD4^+$ and $CD8^+$ wild type T-cells, but was undetectable on $CRP1^{-/-}$ T-cells.

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